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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/980,492	Applicant(s) DIETRICH ET AL.	
	Examiner Humera N. Sheikh	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Receipt of the Amendment filed 06/11/03 is acknowledged.

The 35 U.S.C.112 second paragraph rejection for claims 1-10 have been *withdrawn* by virtue of the amendment.

Claims 1-47 are pending. Claims 1, 9 and 11 have been amended. New claims 21-47 have been added. Claims 1-47 are rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 9-15, 21-22, 25-29, 33-34, 37-41 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Akiyama *et al.* (US Pat. No. 5, 948,773).

Akiyama discloses a pharmaceutical formulation comprising an antibacterial substance and/or an anti-ulcer substance, in that the anti-ulcer substance is a proton pump inhibitor, wherein at least either one of them is formulated into a gastrointestinal mucosa-adherent solid preparation, which comprises a matrix containing a combination mixture of fatty acid esters, lipids and viscogenic agents, whereby lipids include saturated fatty acids or salts thereof, higher alcohols – cetyl alcohol, stearyl alcohol, fatty acid glycerol esters (mono-, di- or triglycerides), waxes, hydrocarbons – paraffin, microcrystalline wax and phospholipids) in combination with pharmaceutically acceptable excipients (see reference column 2, line 16 through col. 3, line 67); (col. 9, line 20 through col. 13, line 59).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 8, 16-20, 23, 24, 30-32, 35, 36, 42-45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akiyama *et al.* (US Pat. No. 5,948,773) in view of Linder *et al.* (US Pat. No. 6,328,993).

Akiyama, as discussed above, teaches a pharmaceutical formulation comprising an antibacterial substance and/or an anti-ulcer substance, in that the anti-ulcer substance is a proton pump inhibitor, wherein at least either one of them is formulated into a gastrointestinal mucosa-adherent solid preparation, which comprises a matrix containing a combination mixture of fatty acid esters, lipids and viscogenic agents, whereby lipids include saturated fatty acids or salts thereof, higher alcohols – cetyl alcohol, stearyl alcohol, fatty acid glycerol esters (mono-, di- or triglycerides), waxes, hydrocarbons – paraffin, microcrystalline wax and phospholipids) in combination with pharmaceutically acceptable excipients (see reference column 2, line 16 through col. 3, line 67); (col. 9, line 20 through col. 13, line 59).

The anti-ulcer substance includes H2 blockers and proton pump inhibitors, wherein proton pump inhibitors are preferred. The proton pump inhibitors include benzimidazole compounds such as lansoprazole, timoprazole, omeprazole and pantoprazole, for example (col. 3, lines 55-67; col. 9, lines 20-34). The salt of a benzimadole compound is preferably used as a physiologically acceptable salt. Physiologically acceptable salts include salts with *inorganic bases*, salts with organic bases and salts with basic amino acids (col. 9, lines 39-49).

The formulation of the invention is used as (1) a combination of an anti-ulcer substance and a gastrointestinal mucosa-adherent solid preparation containing an antibacterial substance, (2) a combination of an antibacterial substance and a gastrointestinal mucosa-adherent solid preparation containing an anti-ulcer substance, (3) a gastrointestinal mucosa-adherent solid preparation containing both an antibacterial substance and an anti-ulcer substance, or (4) a combination of a gastrointestinal mucosa-adherent solid preparation containing an antibacterial substance and a gastrointestinal mucosa-adherent solid preparation containing an anti-ulcer substance. The combination of an anti-ulcer substance and a gastrointestinal mucosa-adherent solid preparation containing an antibacterial substance is preferred (col. 9, lines 53-67).

Akiyama teaches that the matrix containing a polyglyerol fatty acid ester may also incorporate a lipid. The lipid is a water-soluble substance that serves to control the dissolution rate of active ingredients, exemplified by the previously mentioned lipids (col. 13, lines 12-16).

The solid preparation may incorporate additives that include excipients, such as lactose, corn starch, talc, crystalline cellulose; binders, such as sucrose, methyl cellulose, polyvinylypyrrolidone, etc; disintegrating agents, wetting agents, stabilizers and the like (col. 13, lines 28-52).

Example compositions for oral administration include tablets, pills, granules, powders, capsules, syrups, emulsions and suspensions. These compositions are produced by known methods, using lactose, starch, sucrose, magnesium stearate and other substances as carriers or excipients (col. 17, lines 25-29).

Akiyama teaches the inclusion of lipids in the formulation, but is deficient only in the sense that he does not explicitly teach the selected sterols in the formulation.

Linder teaches an administration form comprising acid-labile proton pump inhibitors comprising the use of at least one sterol, whereby suitable sterols include phytosterols, such as ergosterol, stigmasterol, sitosterol, brassicasterol and campesterol and zoosterols, such as cholesterol and lanosterol or mixtures thereof (see reference column 2, line 45 through column 4, line 15).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Linder within the teachings of Akiyama because Linder explicitly teaches that various sterols can be used in the proton pump inhibiting composition and Akiyama teaches also teaches that various lipids can be formulated in the anti-ulcer composition. The expected result would be an improved proton pump inhibiting composition for the effective treatment of disease, as similarly desired by the applicant.

This rejection is maintained and applied to newly added claims 21-47.

Akiyama discloses a proton pump inhibitor pharmaceutical formulation which comprises a matrix containing a combination mixture of fatty acid esters, lipids and viscogenic agents, whereby lipids include saturated fatty acids or salts thereof, higher alcohols – cetyl alcohol, stearyl alcohol, fatty acid glycerol esters (mono-, di- or triglycerides), waxes, hydrocarbons – paraffin, microcrystalline wax and phospholipids)

in combination with pharmaceutically acceptable excipients (column 2, line 16 through col. 3, line 67); (col. 9, line 20 through col. 13, line 59). The proton pump inhibitors include benzimidazole compounds such as lansoprazole, timoprazole, omeprazole and pantoprazole, for example (col. 3, lines 55-67; col. 9, lines 20-34). Oral administration forms include tablets, pills, granules, powders, capsules, syrups, emulsions and suspensions. The granules taught by Akiyama have a particle size of up to approximately 1400 microns.

Akiyama is deficient in the sense that he does not explicitly teach pure enantiomer and esomeprazole.

Linder ('993) obviates this deficiency by teaching acid-labile active proton pump inhibitors wherein the acid-labile proton pump inhibitors also include the pure enantiomers of the acid-labile proton pump inhibitors and their mixtures (see col. 3, lines 58-64). Additionally, Linder teaches at col. 9, claim no. 6, that the acid-labile proton pump inhibitor can be one of esomeprazole.

Regarding the use of the specified solid paraffin, Akiyama teaches the generic concept of adding hydrocarbons, such as paraffins, and thus would include various types of paraffin as those instantly claimed.

With respect to the specified triglyceride (i.e., tristearate, tripalmitate, trimyristate) and fatty acid ester (cetyl palmitate), Akayima recognizes the incorporation of triglycerides, such as monopalmitin and fatty acid esters, such as polyglycerin fatty acid esters of any type. Furthermore, particular ingredients, such as those instantly claimed, could be determined by one of ordinary skill in the art, based on the purpose intended.

Applicants have not shown any unexpected or surprising results that accrue from the use of the instantly named ingredients.

Response to Arguments

Applicant's arguments filed 06/11/03 have been fully considered but they are not persuasive.

Firstly, the applicant argued regarding the 35 U.S.C. 102(e) rejection over Akiyama ('773) stating, "Akiyama relates to a gastrointestinal mucosa-adherent solid preparation, which adheres to a particular site in the gastrointestinal tract. The lipids disclosed comprise a myriad of different types of lipids and no specific combination is disclosed. Akiyama fails to teach each and every element of the claimed invention."

This argument has been fully considered but was not found to be persuasive. Akiyama, as delineated above, discloses a proton pump inhibitor formulation comprising a matrix containing a combination mixture of fatty acid esters, lipids and viscogenic agents, whereby lipids include saturated fatty acids or salts thereof, higher alcohols – cetyl alcohol, stearyl alcohol, fatty acid glycerol esters (mono-, di- or triglycerides), waxes, hydrocarbons – paraffin, microcrystalline wax and phospholipids) in combination with pharmaceutically acceptable excipients. Various proton pump inhibitors include benzimidazole compounds such as lansoprazole, timoprazole, omeprazole and pantoprazole. The applicant's argument that a myriad of different lipids are taught,

however only one is exemplified, is not persuasive since the art recognizes and teaches the generic concept of formulating an array of lipids to control the dissolution rates of the active ingredients. Furthermore, it is not essential that the prior art include multiple examples to demonstrate its particular teaching. It is sufficient that Akiyama recognizes the teaching of similar ingredients for the same field of endeavor and for a similarly intended purpose as the applicants. The instant claims require acid-labile active compounds and excipients, present in a matrix of a mixture of a fatty alcohol and a solid paraffin. The art teaches proton pump inhibitors with excipients in a matrix containing a combination mixture of fatty acid esters, lipids, viscogenic agents, higher and hydrocarbons, such as paraffin. Hence, Akiyama anticipates the instant invention.

Secondly, the applicant argued regarding the 35 U.S.C. 103(a) rejection of Akiyama in view of Linder ('993), stating, "The examiner has failed to establish a *prima facie* case of obviousness against the presently rejected claims. Akiyama fails to teach all the limitations and Linder does not remedy these deficiencies. While Linder teaches a novel administration form for acid-labile active compounds, it does not teach an administration form for acid-labile active compounds comprising pharmaceutical active compounds comprising pharmaceutical excipients and multiple individual active compound units in a matrix comprising at least one fatty alcohol and at least one solid paraffin. Thus the references fail to teach or suggest all the limitations of the claims."

These arguments have been fully considered but were not found to be persuasive. The teachings of Akiyama have been discussed above. Akiyama was lacking in terms of the specified sterol, ester and triglycerides. Linder was relied upon

solely for the teaching of the obviousness of the utilization of various sterols, such as those instantly claimed. Additionally, Linder was referred to for the teaching of pure entantiomers and esomeprazole. The applicants argument that Linder does not teach excipients, nor a matrix comprising multiple active units comprising fatty alcohol and paraffin, is not persuasive since such teachings of a matrix with fatty alcohol and paraffin were already disclosed and demonstrated by Akiyama. Hence, it would not be deemed necessary that Linder disclose each aspect as well, as Akiyama initially taught those particular limitations. Therefore, the prior art clearly establishes a *prima facie* case of obviousness against the instant pending claims.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Akiyama discloses a formulation comprising a proton pump inhibitor comprising a matrix containing a combination mixture of fatty acid esters, lipids, viscogenic agents, higher alcohols, waxes and hydrocarbons in combination with excipients. Akiyama did not disclose the specified sterols or esomeprazole. Linder obviated the use of the specified ingredients (i.e., sterols). As such, the prior art provides ample motivation to use the cited combination of references to formulate a composition as that instantly claimed.

Furthermore, the applicants have not demonstrated any unexpected or surprising results that accrue from the instantly claimed ingredients. The prior art teaches a similar proton pump inhibitor formulation comprising similar ingredients for a functionally equivalent purpose as that desired by the applicants. Hence, the instant invention is rendered obvious and unpatentable over the prior art of record.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

hns
August 21, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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